

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
21 May 2004 (21.05.2004)

PCT

(10) International Publication Number  
**WO 2004/041861 A3**

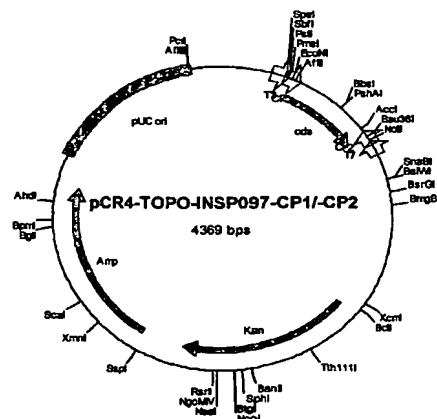
- (51) International Patent Classification<sup>7</sup>: **C07K 14/81**, C12N 15/11, 15/63, 5/10, C12Q 1/68, A61K 38/46, A01K 67/027
- (21) International Application Number: **PCT/GB2003/004786**
- (22) International Filing Date:  
7 November 2003 (07.11.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
0226157.6 8 November 2002 (08.11.2002) GB
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- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,

[Continued on next page]

(54) Title: ALPHA MACROGLOBULIN FAMILY MEMBER

Molecule: pCR4-TOPO-INSP097-CP1/-CP2, 4369 bps DNA Circular

Type	Start	End	Name	Description
MARKER	205		M13R	M13 rev priming site
MARKER	243		T3	T3 priming site
REGION	295	706	Insert	INSP097-CP1/-CP2 PCR product
GENE	295	699	cds	INSP097 receptor binding domain cds
MARKER	295		CP1	INSP097-CP1 PCR primer
MARKER	706		CP2	INSP097-CP2 PCR primer
MARKER	759		T7	T7 priming site
MARKER	782		M13F	M13 for priming site
GENE	1571	2365	Kan	Kanamycin resistance gene ORF
GENE	2569	3429	Amp	Ampicillin resistance gene ORF
REGION	3574	4247	pUC ori	pUC origin



(57) Abstract: This invention relates to a protein, termed INSP097, herein identified as a member of the alpha macroglobulin family, in particular as a alpha-2-macroglobulin-like proteinase inhibitor, and to the use of this protein and nucleic acid sequences from the encoding gene in the diagnosis, prevention and treatment of disease.



KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) **Designated States (regional):** ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- *with international search report*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) **Date of publication of the international search report:**  
1 July 2004

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

# INTERNATIONAL SEARCH REPORT

PCT/GB 03/04786

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/81 C12N15/11 C12N15/63 C12N5/10 C12Q1/68  
A61K38/46 A01K67/027

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N C12Q A01K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, PAJ, WPI Data, EMBL, MEDLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02 079398 A (GORMAN LINDA;BURGESS CATHERINE E ; SPYTEK KIMBERLY A (US); VERNET) 10 October 2002 (2002-10-10) Only the relevant parts of the document are provided claims 1-32; example 26; tables 26D-F	1-15, 19-45
X	NIELSEN K L ET AL: "Amino acid sequence of hen ovomacroglobulin (ovostatin) deduced from cloned cDNA." DNA SEQUENCE: THE JOURNAL OF DNA SEQUENCING AND MAPPING. SWITZERLAND 1994, vol. 5, no. 2, 1994, pages 111-119, XP009027250 ISSN: 1042-5179 abstract; figure 2	1-15, 19-45

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\* & \* document member of the same patent family

Date of the actual completion of the international search

9 March 2004

Date of mailing of the international search report

07/05/2004

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PCT/GB 03/04786

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>NAGASE H ET AL: "OVOSTATIN A NOVEL  PROTEINASE INHIBITOR FROM CHICKEN EGG  WHITE 1. PURIFICATION PHYSICOCHEMICAL  PROPERTIES AND TISSUE DISTRIBUTION OF  OVOSTATIN"  JOURNAL OF BIOLOGICAL CHEMISTRY,  vol. 258, no. 12, 1983, pages 7481-7489,  XP002272798  ISSN: 0021-9258  abstract</p>	<p>1-15,  19-45</p>
A	<p>QAZI USMAN ET AL: "On the structural  changes of native human  alpha2-macroglobulin upon proteinase  entrapment: Three-dimensional structure of  the half-transformed molecule"  JOURNAL OF BIOLOGICAL CHEMISTRY,  vol. 273, no. 15,  10 April 1998 (1998-04-10), pages  8987-8993, XP002272799  ISSN: 0021-9258  cited in the application  abstract</p>	<p>1-15,  19-45</p>

# INTERNATIONAL SEARCH REPORT

PCT/GB 03/04786

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 20, 25-29 are directed to a diagnostic method practised on the human/animal body and claims 30, 35-38 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 16-18 (all completely) and 14, 19-22, 31, 33-37 (all partially)

Present claims 16-18 (all completely) and 14, 19-22, 31, 33-37 (all partially) relate to a compound defined by reference to a desirable characteristic or property, namely binding to alpha-2-macroglobulin-like proteinase inhibitor and increase or decrease of the level of expression or activity of said protein. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to antibodies.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

PCT/GB 03/04786

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 02079398	A	10-10-2002	US 2004002120 A1 01-01-2004
		CA 2440108 A1 10-10-2002	
		EP 1373526 A2 02-01-2004	
		WO 02079398 A2 10-10-2002	
		US 2003207348 A1 06-11-2003	
		CA 2440337 A1 19-09-2002	
		CA 2440345 A1 19-09-2002	
		WO 02072757 A2 19-09-2002	
		WO 02072771 A2 19-09-2002	
		US 2003208039 A1 06-11-2003	
		WO 02072770 A2 19-09-2002	
		US 2003203363 A1 30-10-2003	
		US 2003215449 A1 20-11-2003	
		WO 02070660 A2 12-09-2002	
		US 2003198957 A1 23-10-2003	
		US 2004029116 A1 12-02-2004	